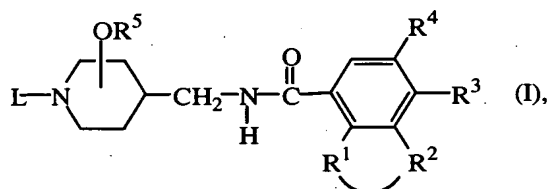


Claims

1. A compound of formula (I)



a stereochemically isomeric form thereof, an *N*-oxide form thereof, or a pharmaceutically acceptable acid or base addition salt thereof, wherein

-R¹-R²- is a bivalent radical of formula

- | | | |
|----|--|--------|
| 10 | -O-CH ₂ -O- | (a-1), |
| | -O-CH ₂ -CH ₂ - | (a-2), |
| | -O-CH ₂ -CH ₂ -O- | (a-3), |
| | -O-CH ₂ -CH ₂ -CH ₂ - | (a-4), |
| | -O-CH ₂ -CH ₂ -CH ₂ -O- | (a-5), |
| 15 | -O-CH ₂ -CH ₂ -CH ₂ -CH ₂ - | (a-6), |
| | -O-CH ₂ -CH ₂ -CH ₂ -CH ₂ -O- | (a-7), |
| | -O-CH ₂ -CH ₂ -CH ₂ -CH ₂ -CH ₂ - | (a-8), |

wherein in said bivalent radicals optionally one or two hydrogen atoms on the same or a different carbon atom may be replaced by C₁₋₆alkyl or hydroxy,

R³ is C₁₋₆alkyl, C₁₋₆alkyloxy, or halo;

R⁴ is hydrogen or halo;

provided that when R³ and R⁴ are both halo, then the bivalent radical-R¹-R²- is of formula (a-5);

R⁵ is hydrogen or C₁₋₆alkyl, and the -OR⁵ radical is situated at the 3- or 4-position of the piperidine moiety;

L is hydrogen, or L is a radical of formula

- | | | |
|----|---|-----------|
| | -Alk-R ⁶ | (b-1), |
| | -Alk-X-R ⁷ | (b-2), |
| | -Alk-Y-C(=O)-R ⁹ | (b-3), or |
| 30 | -Alk-Z-C(=O)-NR ¹¹ R ¹² | (b-4), |

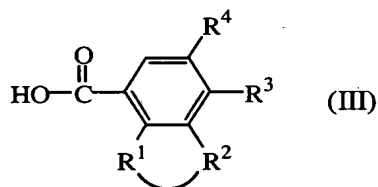
wherein each Alk is C₁₋₁₂alkanediyl; and

R⁶ is hydrogen; hydroxy; cyano; C₃₋₆cycloalkyl; C₁₋₆alkylsulfonylamino; aryl or Het;

R⁷ is C₁₋₆alkyl; C₁₋₆alkyl substituted with hydroxy; C₃₋₆cycloalkyl; aryl or Het;

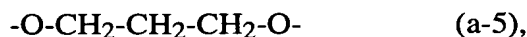
- X is O, S, SO₂ or NR⁸; said R⁸ being hydrogen or C₁₋₆alkyl;
R⁹ is hydrogen, C₁₋₆alkyl, C₃₋₆cycloalkyl, hydroxy or aryl;
Y is a direct bond, or NR¹⁰ wherein R¹⁰ is hydrogen or C₁₋₆alkyl;
Z is a direct bond, O, S, or NR¹⁰ wherein R¹⁰ is hydrogen or C₁₋₆alkyl;
5 R¹¹ and R¹² each independently are hydrogen, C₁₋₆alkyl, C₃₋₆cycloalkyl, or R¹¹ and R¹² combined with the nitrogen atom bearing R¹¹ and R¹² may form a pyrrolidinyl, piperidinyl, piperazinyl or 4-morpholinyl ring both being optionally substituted with C₁₋₆alkyl;
aryl represents unsubstituted phenyl or phenyl substituted with 1, 2 or 3 substituents
10 each independently selected from halo, hydroxy, C₁₋₆alkyl, C₁₋₆alkyloxy, C₁₋₆alkylcarbonyl, nitro, trifluoromethyl, amino, aminocarbonyl, and aminosulfonyl; and
Het is furanyl; furanyl substituted with C₁₋₆alkyl or halo;
tetrahydrofuranyl; tetrahydrofuranyl substituted with C₁₋₆alkyl;
15 dioxolanyl; dioxolanyl substituted with C₁₋₆alkyl;
dioxanyl; dioxanyl substituted with C₁₋₆alkyl;
tetrahydropyranyl; tetrahydropyranyl substituted with C₁₋₆alkyl;
2,3-dihydro-2-oxo-1H-imidazolyl; 2,3-dihydro-2-oxo-1H-imidazolyl substituted with one or two substituents each independently selected from
20 halo, or C₁₋₆alkyl;
pyrrolidinyl; pyrrolidinyl substituted with one or two substituents each independently selected from halo, hydroxy, or C₁₋₆alkyl;
pyridinyl; pyridinyl substituted with one or two substituents each independently selected from halo, hydroxy, C₁₋₆alkyl;
25 pyrimidinyl; pyrimidinyl substituted with one or two substituents each independently selected from halo, hydroxy, or C₁₋₆alkyl;
pyridazinyl; pyridazinyl substituted with one or two substituents each independently selected from hydroxy, C₁₋₆alkyloxy, C₁₋₆alkyl or halo;
pyrazinyl; pyrazinyl substituted with one or two substituents each
30 independently selected from hydroxy, C₁₋₆alkyloxy, C₁₋₆alkyl or halo.
2. A compound as claimed in claim 1 wherein the -OR⁵ radical is situated at the 3-position of the piperidine moiety having the trans configuration.
- 35 3. A compound as claimed in claim 2 wherein the absolute configuration of said piperidine moiety is (3S, 4S).

4. A compound as claimed in any of claims 1 to 3 wherein $-R^1-R^2-$ is a radical of formula (a-5), R^3 is chloro and R^4 is chloro.
5. A compound as claimed in any of claims 1 to 3 wherein $-R^1-R^2-$ is a radical of formula (a-5), R^3 is chloro and R^4 is bromo.
6. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically active amount of a compound according to any of claims 1 to 5.
7. A process for preparing a pharmaceutical composition according to claim 6 wherein a therapeutically active amount of a compound according to any of claims 1 to 5 is intimately mixed with a pharmaceutically acceptable carrier.
8. A compound according to any of claims 1 to 5 for use as a medicine.
9. A compound of formula (III)



wherein

- 20 $-R^1-R^2-$ is a bivalent radical of formula

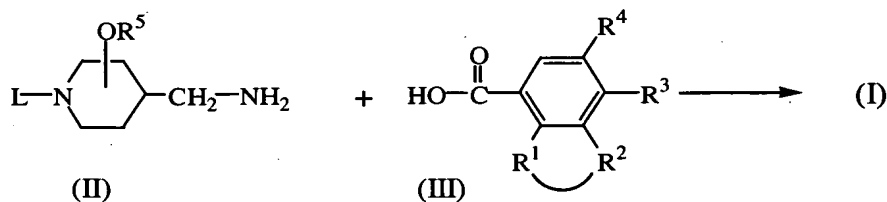


wherein in said bivalent radicals optionally one or two hydrogen atoms on the same or a different carbon atom may be replaced by C_{1-6} alkyl or hydroxy;

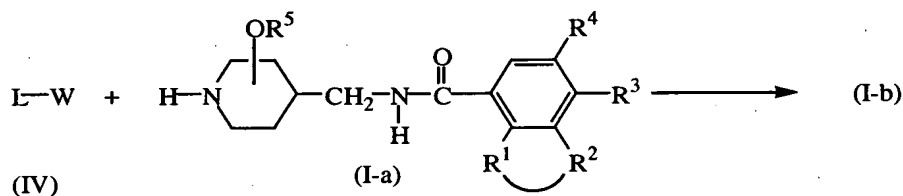
R^3 is C_{1-6} alkyl, C_{1-6} alkyloxy, or halo; and

R^4 is hydrogen or halo.

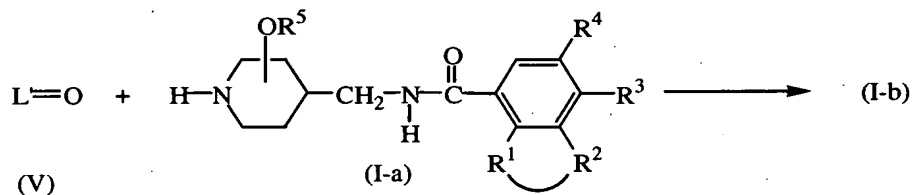
10. A process for preparing a compound of formula (I) wherein
 - a) an intermediate of formula (II) is reacted with an carboxylic acid derivative of formula (III) or a reactive functional derivative thereof;



- b) an intermediate of formula (IV) is *N*-alkylated with a compound of formula (I-a), defined as a compound of formula (I) wherein L represents hydrogen, in a reaction-inert solvent and, optionally in the presence of a suitable base, thereby yielding compounds of formula (I-b), defined as compounds of formula (I) wherein L is other than hydrogen;



- c) an appropriate ketone or aldehyde intermediate of formula L'=O (V), said L'=O being a compound of formula L-H, wherein two geminal hydrogen atoms in the C₁₋₁₂alkanediyl moiety are replaced by =O, is reacted with a compound of formula (I-a), thereby yielding compounds of formula (I-b);



wherein in the above reaction schemes the radicals -R¹-R²-, R³, R⁴ and R⁵ are as defined in claim 1 and W is an appropriate leaving group;

- d) or, compounds of formula (I) are converted into each other following art-known transformation reactions; or if desired; a compound of formula (I) is converted into a pharmaceutically acceptable acid addition salt, or conversely, an acid addition salt of a compound of formula (I) is converted into a free base form with alkali; and, if desired, preparing stereochemically isomeric forms thereof.